

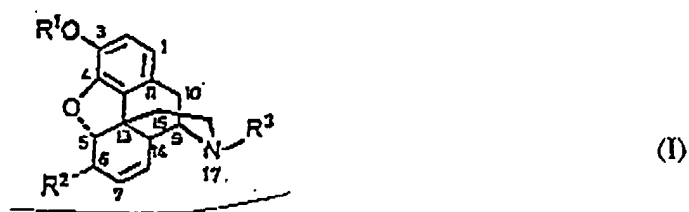
Docket No. F-6826

Ser. No. 09/508,907

**AMENDMENTS TO THE CLAIMS:**

Please replace the claims with the claims provided in the listing below wherein status, amendments, additions and cancellations are indicated.

1. (Currently amended) Transdermal or transmucosal composition for administering at least one morphine alkaloid, the composition comprising at least one morphine alkaloid each as the acid addition salt thereof with an organic acid, each said morphine alkaloid being of the following Formula I:



where  $R^1$  is selected from the group consisting of H,  $C_1$ - to  $C_6$ -alkyl residues;  $R^2$  is selected from the group consisting of the monad residues H, OH,  $OC(O)CH_3$ , whereby in this case the fourth valence of the (6)-C atom is occupied by H, or the dyad residues  $=O$ ,  $=CH_2$ ;  $R^3$  is selected from the group consisting of  $-CH_3$ , cyclopropyl, cyclobutyl and allyl;

the organic acid being selected from

Docket No. F-6826

Ser. No. 09/508,907

monoesters of  $C_3$ - to  $C_{16}$ -dicarboxylic acids with monohydric  $C_1$ - to  $C_4$ -alcohols,

$C_2$ - to  $C_6$ - and  $C_8$ - to  $C_{16}$ -sulfonic acids,

substituted benzoic acids, selected from the group consisting of halogen, hydroxy p- and m-hydroxy, alkyl, hydroxyalkyl, alkoxyalkyl, alkoxy-substituted benzoic acids, aminosubstituted benzoic acids, aminosubstituted benzoic acids alkylated at the N atom,

substituted or unsubstituted 5-ring or 6-ring heterocycles comprising at least one N or S atom and having a carboxyl group function or branched or unbranched carboxypropyl or carboxybutyl groups as substituents,

saturated or unsaturated, substituted or unsubstituted, oxocarboxylic acids having 5 to 10 C atoms,

~~phenyl-substituted or phenoxy-substituted~~ saturated  $C_2$ - to  $C_4$ -carboxylic acids,

Docket No. F-6826

Ser. No. 09/508,907

aliphatic, aromatic or heterocyclic C<sub>2</sub>- to C<sub>12</sub>-amino acids, wherein one amino group is substituted with a substituted or unsubstituted C<sub>2</sub>- to C<sub>6</sub>-alkanoyl group or a substituted or unsubstituted benzoyl group,

the acid salt having a property of penetrating skin as defined by a flux of at least 2.34  $\mu\text{g}/\text{cm}^2$  h.

2. (Previously presented) Composition according to Claim 1, wherein the organic acid is selected from aliphatic monoaminomonocarboxylic acids, wherein the amino group is substituted with an unsubstituted C<sub>2</sub>- to C<sub>6</sub>-alkanoyl group or with a C<sub>2</sub>- to C<sub>6</sub>-alkanoyl group which is monosubstituted or polysubstituted with hydroxy, C<sub>1</sub>- to C<sub>4</sub>-alkoxy- or C<sub>1</sub>- to C<sub>4</sub>-hydroxyalkyl, or wherein the amino group is substituted with an unsubstituted benzoyl residue or with benzoyl residue which is mono- or polysubstituted with C<sub>1</sub>- to C<sub>4</sub>-alkyl, C<sub>1</sub>- to C<sub>4</sub>-alkoxy, C<sub>1</sub>- to C<sub>4</sub>-hydroxyalkyl, halogen, amino or hydroxy.

3. (Previously presented) Composition according to Claim 2, wherein the organic acid is selected from aliphatic C<sub>2</sub>- to C<sub>6</sub>-monoaminomonocarboxylic acids, wherein the amino group is substituted with an acetyl group or a benzoyl group.

Docket No. F-6826

Ser. No. 09/508,907

4. (Currently amended) Composition according to Claim 1, wherein the organic acid is selected from:

hydroxy- ( $C_1$ - to  $C_4$ )-alkyl,  $C_1$ - to  $C_6$ -alkoxy-( $C_1$ - to  $C_4$ )-alkyl-substituted or p- or m-hydroxy-substituted benzoic acids,

monoesters of  $C_5$ - to  $C_{10}$ -dicarboxylic acids,

$C_4$ - to  $C_6$ -and  $C_8$ -sulfonic acids.

5. (Previously amended) Composition according to Claim 1, wherein the acid is selected from  $C_1$ - to  $C_4$ -alkyl-substituted benzoic acids.

6. (Previously amended) Composition according to Claim 1, wherein the organic acid is hexanesulfonic acid, aminobenzoic acid or trimethylbenzoic acid.

7. (Previously amended) Composition according to Claim 1, wherein the 5-ring or 6-ring heterocycle is a pyridine-carboxylic acid.

Docket No. F-6826

Ser. No. 09/508,907

8. (Previously amended) Composition according to Claim 1, wherein the oxocarboxylic acid is a saturated or unsaturated 2-, 4-, 5- or 9-oxocarboxylic acid.

9. (Previously amended) Composition according to Claim 8, wherein the oxocarboxylic acid is 5-oxopyrrolidine-2-carboxylic acid, levulic acid or oxodec-2-ene acid.

10. (Previously amended) Composition according to Claim 3, wherein the organic acid is acetylglycin or hippuric acid.

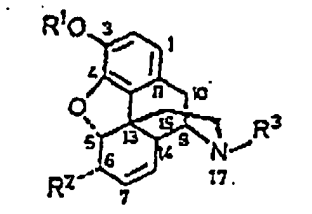
11. (Previously amended) Composition according to any one of Claims 1 to 10 and 17 to 25, wherein the morphine alkaloid is morphine, codeine, heroin, ethylmorphine, levorphanol or hydromorphone.

12. (Previously amended) Composition according to Claim 1, comprising a solution or suspension of the acid addition salt in glycerin, ethylene glycol, dimethyl isosorbide, oleic acid and/or dimethyl sulfoxide.

13. (Previously amended) Acid addition salts of morphine alkaloid and organic acid, said morphine alkaloid having the following Formula 1:

Docket No. F-6826

Ser. No. 09/508,907



(I)

where  $R^1$  is selected from the group consisting of H,  $C_1$ - to  $C_6$ -alkyl residues;  $R^2$  is selected from the group consisting of the monad residues H, OH,  $OC(O)CH_3$ , whereby in this case the fourth valence of the (6)-C atom is occupied by H, or the dyad residues  $=O$ ,  $=CH_2$ ;  $R^3$  is selected from the group consisting of  $-CH_3$ , cyclopropyl, cyclobutyl and allyl;

the organic acid being selected from

monoesters of  $C_3$ - to  $C_{16}$ -dicarboxylic acids with monohydric  $C_1$ - to  $C_4$ -alcohols,

$C_2$ - to  $C_6$ - and  $C_8$ - to  $C_{16}$ -sulfonic acids,

Docket No. F-6826

Ser. No. 09/508,907

halogen, p- and m-hydroxy, alkyl, hydroxyalkyl, alkoxyalkyl and/or alkoxy-substituted benzoic acids, aminosubstituted benzoic acids, aminosubstituted benzoic acids alkylated at the N atom,

substituted or unsubstituted 5-ring or 6-ring heterocycles comprising at least one N or S atom and having a carboxyl group function or branched or unbranched carboxypropyl or carboxybutyl groups as substituents,

saturated or unsaturated, substituted or unsubstituted, oxocarboxylic acids having 5 to 10 C atoms,

phenoxy-substituted saturated C<sub>2</sub>- to C<sub>4</sub>-carboxylic acids,

aliphatic, aromatic or heterocyclic C<sub>2</sub>- to C<sub>12</sub>-amino acids, wherein one amino group is substituted with a substituted or unsubstituted - C<sub>2</sub>- to C<sub>6</sub>-alkanoyl group or a substituted or unsubstituted benzoyl group

the acid salt having a property of penetrating skin as defined by a flux of at least 2.34  $\mu\text{g}/\text{cm}^2 \text{ h}$ .

Docket No. F-6826

Ser. No. 09/508,907

14. (Previously amended) Method for the production of acid addition salts according to Claim 13, comprising the steps of providing a solution of the morphine alkaloid, reacting, in a further step, said solution with equimolar amounts of a solution of the organic acid and isolating the resultant addition salt.

15. (Cancelled)

16. (Previously presented) A lotion, ointment, creme, gel, spray, iontophoretic device, transmucosal therapeutic system or transdermal therapeutic system, the transdermal therapeutic system including a backing layer which is permeable or impermeable with respect to the active substance, and a reservoir layer, comprising a composition according to Claim 1.

17. (Previously presented) Composition according to Claim 1, wherein the alkyl residues are selected from methyl, ethyl, propyl, i-propyl and  $C(OH)CH_3$ .

18. (Previously presented) Composition according to Claim 1, wherein the bond at  $C_7/C_8$  is saturated.



Docket No. F-6826

Ser. No. 09/508,907

19. (Previously presented) Composition according to Claim 1, wherein a nitroxyl group is present at N<sub>17</sub>.

20. (Previously presented) Composition according to Claim 1, wherein the alcohol of the monoester is methanol.

21. (Previously presented) Composition according to Claim 1, wherein the carbonyl group function of the 5-ring or 6-ring heterocycles is selected from carboxy, carboxymethyl and carboxyethyl.

22. (Previously presented) Composition according to Claim 21, wherein the dicarboxylic acids of the monoesters are suberic acid, azelaic acid and sebacic acid.

23. (Previously presented) Composition according to Claim 4, wherein the sulfonic acid is hexanesulfonic acid.

24. (Previously presented) Composition according to Claim 5, wherein the acid is selected from C<sub>1</sub>- to C<sub>4</sub>-trialkyl-substituted benzoic acids.

Docket No. F-6826

Ser. No. 09/508,907

25. (Previously presented) Composition according to Claim 7, wherein the pyridine-carboxylic acid is nicotinic acid or lipoic acid.

26. (Previously presented) Acid addition salts according to Claim 13, wherein the alkyl residues are selected from methyl, ethyl, propyl, i-propyl and  $C(OH)CH_3$ .

27. (Previously presented) Acid addition salts according to Claim 13, wherein the bond at  $C_7/C_8$  is saturated.

28. (Previously presented) Acid addition salts according to Claim 13, wherein a nitroxyl group is present at  $N_{17}$ .

29. (Previously presented) Acid addition salts according to Claim 13, wherein the alcohol of the monoester is methanol.

30. (Previously presented) Acid addition salts according to Claim 13, wherein the carboxyl group function of the 5-ring or 6-ring heterocycles is selected from carboxy, carboxymethyl and carboxyethyl. -